DETAILED ACTION

Response to Amendments/Arguments

Applicant's amendments to the claims and specification filed January 28, 2008 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below in original or modified form is herein withdrawn. Applicant has cancelled all pending claims, thus the rejections are withdrawn as moot. It is noted that 10/462,452 has been abandoned, thus the ODP rejection is withdrawn as moot.

The current restriction is amended to reflect that claim 93 is a linking claim is now the linking claim linking the inventions of SEQ ID NOs: 32-35 and 42 as currently drafted. Applicant has elected the invention drawn to SEQ ID NO:42, readable upon claims 93, 94, 99-113.

Election/Restrictions

Applicant has elected the species of the 'biologically active agent' as PTH, which reads upon claims 93, 94, 99-100, 103, 104 and 107-113. During examination and search, the examiner found additional species of the active agent, readable upon claims 101, 105 and 106, thus they have been included (below).

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, and Applicant has not indicated the election was made 'with' or 'without' traverse, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 95-98 and 102 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. The restriction is still deemed proper and made FINAL.

Claim Objections

Claim 103 is objected to because of the following informalities: The claim contains a spelling error 'gonadotropin' is misspelled 'gonadotrohin'. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 103 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 103 recites that the biologically active agent is a protein or peptide, however the claim recites non peptide/protein species, and thus it is unclear as to the definition of what a peptide/protein is intended to be or as to what are the intended metes and bounds of the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 93, 94, 99-101 and 104 are rejected under 35 U.S.C. 102(b) as being anticipated by BLASCHUK (WO 99/35166 A1).

Blaschuk teaches a pharmaceutical composition comprising: A) a CAM agent, where the CAM agent is either QYLYHYCVVD or YLYHYCVVD- both readable upon comprising and consisting of the elected invention instant SEQ ID NO:42; and B) a 'drug' (e.g. claim 44), where drug is defined in the specification as, "any bioactive agent intended for administration to a mammal to prevent or treat a disease or other undesirable condition. Drugs include hormones,

growth factors, proteins, peptides and other compounds." (page 39, lines 16-20). Blaschuk exemplifies a variety of drug classes (spanning page 40, lines 18 to page 41 line 5), including antimicrobials, antiinflammatories, analgesics, toxins, tranquilizers and hypnotics. Blaschuk exemplifies morphine (page 47, line 29), insulin (page 48, line 7), gentamycin (page 48, line 12), digoxin in combination with furosemide (page 49, line 16), indomethacin, prednisone, morphine, codeine, demerol, acetaminophen, vancomycin, heparin, and others (spanning pages 49 and 50).

Blaschuk teaches that, "Numerous other drugs may be administered as described herein, including naturally occurring and synthetic hormones, growth factors, proteins and peptides. For example, insulin and human growth hormone, growth factors like erythropoietin, interleukins and interferons may be delivered via the skin." (page 50, lines 19-22). Blaschuk teaches a kit for transdermal delivery, e.g. a skin patch (spanning pages 47 -50).

Blaschuk teaches that the composition comprises one or more modulating agents in combination with one or more pharmaceutically or physiologically acceptable carriers, diluents or excipients (spanning page 39, lines 22 to page 40, line 6), including buffers (e.g. neutral buffered saline or PBS), carbohydrates, mannitol (a sugar alcohol), proteins, polypeptides or amino acids, antioxidants, chelating agents, e.g. EDTA or GSH, adjuvants and/or preservatives. Blashchuk additionally teaches that the composition may be encapsulated into a liposome, "using well known technology."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 93, 94, 99-101, 104-108, 110 and 111 are rejected under 35 U.S.C. 103(a) as being unpatentable over BLASCHUK, *supra*.

The teachings of Blaschuk are presented *supra*.

While Blaschuk teaches all elements of the composition (the peptide with a drug) and various examples, Blaschuk does not specifically teach a composition with a specific drug, e.g. apomorphine or a derivative. Morphine is considered a derivate of apomorphine, as is codeine. Further, Blaschuk provides general teachings as to what additional elements are within the composition, e.g. buffer, etc., however Blaschuk does not specifically teach a composition with the additional elements.

It would have been obvious to have formulated the composition with any drug, including morphine, insulin, gentamycin or any of the other drugs of Blaschuk, as they are contemplated for use in the composition therein. Further, it would have been obvious to have used any additional elements contemplated by Blaschuk in the composition, including a chelator, e.g. EDTA, a buffer, e.g. PBS (equivalent to 'a pH control agent'), an alcohol, e.g. mannitol, as well as to encapsulated the composition in a liposome. One would have found sufficient motivation and guidance based upon the specific teachings of Blaschuk to formulate the compositions with any of the compounds recited with the expectation of forming a composition for transdermal delivery, as described by Blaschuk.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 93, 94, 99-101, 103-108, 110 and 111 are rejected under 35 U.S.C. 103(a) as being unpatentable over BLASCHUK, as applied to claims 93, 94, 99-101, 104-108, 110 and 111 *supra*, in view of OCHILICH (WO 96/35447 A1).

The teachings of Blaschuk are presented *supra*. Blaschuk does not teach PTH as the drug.

Ochilich teaches transdermal delivery of PTH as the active agent as a patch comprising permeation accelerators to control release of the active ingredient and permeation through the skin (page 3, lines 1-7).

It would have been obvious to have used the composition of Blaschuk in the transdermal delivery system of Ochilich in order to deliver any drug, including PTH, as Ochilich teaches permeation accelerators should be used in the transdermal delivery method to ensure continuous release and permeation through the skin. One would have been motivated to have used the composition of Blaschuk as the transdermal delivery composition, as it Blaschuk teaches the

composition can be used to deliver any type of drug, including hormones, as a convenient method of administration of a slow release compositions. One would reasonably expect the composition of Blaschuk to be amenable to delivery of PTH, or any other drug, given the teachings therein with regards to formulation with any compound, including hormones, and the teachings of Ochilich that show PTH transdermal delivery should include penetration enhancing/delivery enhancing compositions.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 93, 94, 99-101 and 103-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over BLASCHUK in view of OCHILICH, as applied to claims 93, 94, 99-101, 103-108, 110 and 111 *supra*, in further view of HANSEN (US Patent 5,120,546).

The teachings of Blaschuk and Ochilich are presented *supra*. While Blaschuk teaches carbohydrates can be used in the composition, Blaschuk does not teach cyclodextrin or β-cyclodextrin derivative in the composition.

Hansen teaches the use of cyclodextrin in transdermal delivery systems to control release of a drug (throughout). Hansen teaches, "It is previously known to use cyclodextrins in transdermal systems. The most important purposes for these compounds have been used is to achieve superior properties as to solubility, releasing properties, stability, bioavailability and efficacy of certain active substances… It is thus previously known that active substances, e.g. drugs, can be included in transdermal patches in the form of cyclodextrin complexes for various reasons." (spanning columns 2 and 3).

Thus it would have been obvious to have use cyclodextrin as the carbohydrate in the transdermal composition of Blaschuk to obtain the superior properties as to solubility, releasing properties, stability, bioavailability and efficacy. One would have been motivated to have used cyclodextrin for these same reasons. One would have a reasonable expectation that these benefits, well known to the artisan, would be beneficial in a transdermal delivery system, particularly one that provides guidance as to the inclusion of a carbohydrate as a component.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 93, 94, 99-101 and 103-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over BLASCHUK in view of OCHILICH and HANSEN, as applied to claims 93, 94, 99-101 and 103-111 *supra*, in further view of KIM (WO 01/87276 A1).

The teachings of Blaschuk, Ochilich and Hansen are presented *supra*. Blaschuk, while teaching additional elements can be present, does not teach a long-chain amphipathic molecule or a medium-chain fatty acid (MCFA).

Kim teaches permeation enhancers for transdermal delivery in a hydrogel composition, including solvents such as alcohols (page 8, lines 13-18), saturated and unsaturated fatty acids, e.g. oleic acid (page 8, lines 3-9), and C_8-C_{18} saturated and unsaturated fatty acids (e.g. page 11, lines 7-13).

It would have been obvious to have included any additional agent into the composition of Blaschuk, including a MCFA or long-chain amphipathic molecule, e.g. oleic acid, as the composition of Blaschuk allows for the inclusion of additional permeation enhancers. Further, one would have been motivated to have included an additional permeation enhancer to the composition to facilitate controlled transport across the skin, as such elements are known to the artisan to be useful to be included in the transdermal delivery composition (Kim page 12, lines 22-26). One would have a reasonable expectation of obtaining the benefit of controlled transport given the teachings of Kim.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims

would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 93, 94, 99-101 and 103-113 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 34-80 of copending Application No. 10/840,536 (QUAY(2), US 2004/02586663 A1; amended claim set of 7/30/07).

Quay(2) teaches compositions which are of an overlapping, if not commensurate scope, where the composition is interferon-α with one or more mucosal delivery agents, formulated for nasal delivery as a powder or spray, comprising mucosal delivery-enhancing agents which overlap with the instant composition, where the mucosal delivery-enhancing agent is a JAM protein. In looking to the specification for JAM proteins which provide support for the claims, Quay(2) specifically identifies the peptides of the instant application as JAM peptides (e.g. paragraphs [0199] and [0200]).

This is a provisional obviousness-type double patenting rejection.

Claims 93, 94, 99-101 and 103-113 are directed to an invention not patentably distinct from claims 34-80 of commonly assigned 10/840,536, for the reasons set forth *supra*.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 10/840,536 discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly

assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Applicant is reminded that due to Applicant's prolific Patent and Application portfolio, the burden is shifted to Applicant to identify all relevant Applications and Patents and to include said Applications and Patents on any terminal disclaimer filed.

Conclusion

The prior art made of record as cited on the enclosed PTO-892 and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Andrew D Kosar/
Primary Examiner, Art Unit 1654